REMARKS

A check in the amount of $180.00 for the fee for a supplemental Information Disclosure Statement accompanies this Amendment. Any fees that may be due in connection with this paper, or with this application throughout its pendency, may be charged to Deposit Account No. 50-1213. If a Petition for an Extension of Time in required, this paper is to be considered such Petition.

Claims 1-61, 65-67, 71-73, 77-89 and 92-99 are pending. Claim 8 is amended herein to correct an obvious typographical error. No new matter has been added and no subject matter has been surrendered thereby.

The specification is amended to correct obvious typographical, spelling and formatting errors and to produce grammatical clarity. In particular the amendments to the paragraph page 3, line 3-10, adds an inadvertently omitted known formula of RPR 106541 (see, *e.g.*, Warne (2000) *Emerging Drugs 5(2)*:231-239, copy enclosed with Supplemental Information Disclosure Statement). No new matter has been added. Included as an attachment is a marked-up version of the specification paragraphs and claims, per 37 CFR §1.121.

A supplemental Information Disclosure Statement is also attached to this Amendment.

A Change of Address Notification accompanies this Amendment.

TRAVERSAL OF RESTRICTION REQUIREMENT

A Restriction Requirement issued in this application on January 30, 2002, setting forth four Groups for election. Applicant elected Group I, with traverse, in an Election and Preliminary Amendment filed February 28, 2002. The instant Office Action states that Applicant's traverse of the Restriction Requirement is not found persuasive and has made the Requirement Final. Applicant filed a Petition under 37 C.F.R. §1.144 requesting reconsideration and removal of the Restriction Requirement as between Group I and Group II (in part), and as

between Group I and Group IV, on July 22, 2002. Applicant provides the following remarks for the Examiner's consideration.

Applicant respectfully submits that Group I is related to each of Groups II (in part, claims 65-67, 92 and 93) and IV as a subcombination/combination for which a showing of two-way distinctness is required.

Inventions that are related as a combination and subcombination are distinct and restriction may be proper **only if** it can be shown that the combination as claimed does not require the particulars of the subcombination as claimed for patentability **and** that the subcombination has utility by itself or in other combinations. See MPEP 808.05(c).

If the compositions of Group I are deemed free of the prior art, the combinations of Group II and the articles of manufacture of Group IV, which contain the compositions of Group I, will necessarily be free of the prior art. Therefore, the combinations of claims 65-67, 92 and 93 of Group II and compositions of Group I are not distinct, and the articles of manufacture of Group IV and the compositions of Group I are not distinct.

If the claims are restricted into these three groups, applicant ultimately could be granted three patents: (i) one that includes claims encompassing pharmaceutical compositions; (ii) another with claims directed to combinations containing the compositions; and (iii) a third with claims directed to articles of manufacture that contain the compositions, that expire on different dates. If the claims to the combinations (combinations of Group II containing a composition and a vial, and articles of manufacture of Group IV) issued first, a later issuing patent encompassing the subcombination (compositions of Group I) could not be held to constitute obvious-type double patenting over the earlier issuing patent. See MPEP 806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Where restriction is required by the Office double patenting cannot be held, and thus, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP 804.01, which states:

> 35 U.S.C. 121 authorizes the Commissioner to restrict the claims in a patent application to a single invention when independent and distinct inventions are presented for examination. The third sentence of 35 U.S.C. 121 prohibits the use of a patent issuing on an application with respect to which a requirement for restriction has been made, or on an application filed as a result of such a requirement, as a reference against any divisional application, if the divisional application is filed before the issuance of the patent. The 35 U.S.C. 121 prohibition applies only where the Office has made a requirement for restriction. The prohibition does not apply where the divisional application was voluntarily filed by the applicant and not in response to an Office requirement for restriction. This apparent nullification of double patenting as a ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restrictions where the claims define essentially the same invention in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

Therefore, restriction of Group I and claims 65-67, 92 and 93 of Group II, and of Groups I and IV, is improper. Applicant respectfully requests reconsideration and removal of the Restriction Requirement as between these Groups.

INFORMATION DISCLOSURE STATEMENT

The Office Action alleges that the Information Disclosure Statement, filed February 11, 2002 fails to comply with 37 C.F.R. §1.98(a)(3) because it allegedly does not contain a concise explanation of the relevance of each patent listed that is not in the English language. Applicant respectfully requests reconsideration of the refusal to enter the Information Disclosure Statement in view of the comments below, or, alternatively, requests that the remaining documents cited in the Information Disclosure Statement be considered.

Applicant presumes that the reference in question is German Patent No. DE 2,305,092 (Item AF). As stated in the Information Disclosure Statement, a Derwent English-language Abstract (Item AL) of this reference was also submitted. MPEP 609, part III.A(3), paragraph 2, states:

> ...Submission of an English language abstract of a reference may fulfill the requirement for a concise explanation...

Applicant respectfully submits that the requirement for a concise explanation has been fulfilled by the concurrent filing of the corresponding Derwent English-language Abstract. Therefore, this reference, and all the references provided in the Information Disclosure Statement, should have been considered. Applicant respectfully requests that the Examiner consider the references cited in the Information Disclosure Statement and that they be made of record herein.

Alternatively, Applicant respectfully submits that, even if the refusal to consider the German reference was proper, the remaining references should have been considered. MPEP 609, part III.C(1), paragraph 4, states:

> If an item of information in an IDS fails to comply with all the requirements of 37 CFR 1.97 and 37 CFR 1.98, that item of information in the IDS will not be considered and a line should be drawn through the citation to show that it has not been considered. *However, other items of information that do comply with all the requirements of 37 CFR 1.97 and 37 CFR 1.98 will be considered by the examiner.* (emphasis added)

Thus, at the very least, Items A-AE and AG-BD should have been considered and entered into the record. Applicant respectfully requests that these items, at the very least, be considered by the Examiner and entered into the record.

REJECTION OF CLAIM 1 UNDER 35 U.S.C. §102(e)

Claim 1 is rejected under 35 U.S.C. §102(e) as allegedly being anticipated by the disclosure of Adjei *et al.* (U.S. Patent No. 6,261,539). It is alleged that Adjei *et al.* teaches a aerosol formulation containing a particulate medicament, such as formoterol, and water, and thus anticipates the instant claim. Applicant respectfully traverses this rejection.

Relevant Law

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir, 1990), *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990), *Soundscriber Corp. v. U.S.*, 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), *cert. denied*, 110 S.Ct. 154 (1989). "[A]ll

limitations in the claims must be found in the reference, since the claims measure the invention." *In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover, it is incumbent on the Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. *Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). "Rejections under 35 U.S.C. §102 are proper only when the claimed subject matter *is* identically disclosed or described in the "'prior art'" "...the [r]eference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings in the cited references. Such picking and choosing may be entirely proper when making a rejection of a 103, obviousness rejection, where the applicant must be afforded an opportunity to rebut with objective evidence any inference of obviousness which may arise from the *similarity* of the subject matter which he claims to the prior art, but it has no place in the making of a 102, anticipation rejection." [Emphasis in original]. *In re Arkey, Eardly, and Long*, 455 F.2d 586, 172 USPQ 524 (CCPA 1972).

Instant claim 1

Instant claim 1 is directed to a pharmaceutical composition, containing formoterol, or a derivative thereof, *in a pharmacologically suitable fluid*, wherein the composition is stable during long term storage and the fluid comprises water. (emphasis added)

Differences between the disclsoure of Adjei *et al.* and instant claim 1

Adjei *et al.* discloses compositions containing a particulate medicament, such as formoterol; a propellant; and a stabilizer consisting of water. Adjei *et al.* does not disclose compositions containing a pharmacologically suitable fluid, as defined in the instant application. See, page 8, lines 10-13:

> As used herein, a pharmacologically suitable fluid is a solvent suitable for pharmaceutical use *which is not a liquified propellant gas*. Exemplary pharmacologically suitable fluids include polar fluids, including protic fluids such as water. (emphasis added)

Thus, Adjei *et al.* does not disclose any compositions within the scope of instant claim 1. The compositions of Adjei *et al.* contain a propellant. The compositions of the instant claims do not contain a propellant. Therefore, the disclosure of Adjei *et al.* does not anticipate the instant claims.

REJECTION OF CLAIMS 4-61, 77-79 AND 94-99 UNDER 35 U.S.C. §103(a)

Claims 4-61, 77-79 and 94-99 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over the teachings of Adjei *et al.* The Office Action alleges that, while the cited reference does not teach the amounts of the components of the compositions recited in the instant claims, determination of optimal amounts would have been within the level of one of ordinary skill in the art. Applicant respectfully traverses this rejection.

Relevant Law

[I]n order to establish a *prima facie* case of obviousness, there must be evidence, preferably a teaching, suggestion, incentive or inference from the cited art or in the form of generally available knowledge that one of ordinary skill would have been led to modify the relevant teaching to arrive at what is claimed. *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963).

The prior art must provide a motivation whereby one of ordinary skill in the art would have been led to do that which the applicant has done. *Stratoflex Inc. v Aeroquip Corp.*, 713 F.2d 1530, 1535, 218 USPQ 871, 876 (Fed. Cir. 1983). In addition, the mere fact that the prior art may be modified in the

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manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification. *In re Fritch*, 23 USPQ 1783 (Fed. Cir. 1992).

In addition, unexpected properties must always be considered in the determination of obviousness. A compound's structure and properties are inseparable so that unexpected properties are part of the subject matter as a whole. *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963).

The instant claims

Instant claim 4 is directed to the pharmaceutical composition of claim 1 (*supra*) that has been nebulized. Claim 5 is directed to the pharmaceutical composition of claim 1, where the pharmacologically suitable fluid contains a polar solvent. Claim 6 is directed to the pharmaceutical composition of claim 5, where the polar solvent is a protic solvent.

Instant claims 7-43, 49-60, 78 and 79 are directed to pharmaceutical compositions of claims 1 or 6 that further contain a tonicity adjusting agent and/or a buffer, and that have the recited ionic strength, pH and/or formoterol concentration.

Claims 44-48 are directed to pharmaceutical compositions that have been nebulized.

Claim 61 is directed to a nebulized solution, containing formoterol or a derivative thereof in a pharmacologically suitable fluid.

Claim 77 is directed to the pharmaceutical composition of claim 1, further containing one or more of (a) to (j) as follows: (a) a β_2-adrenoreceptor agonist; (b) a dopamine (D_2) receptor agonist; (c) an IL-5 inhibitor; (d) an antisense modulator of IL-5; (e) a tryptase inhibitor; (f) a tachykinin receptor antagonist; (g) milrinone or milrinone lactate; (h) a leukotriene receptor antagonist; (i) a 5-lypoxygenase inhibitor; or (j) an anti-IgE antibody.

Claims 94-99 are directed to the pharmaceutical composition of claim 1, further containing an anticholinergic agent, such as ipratropium bromide,

oxitropium bromide, atropine methyl nitrate, tiotropium bromide or glycopyrronium bromide.

The teachings of Adjei *et al.* and differences from the instant claims

Adjei *et al.* teaches compositions containing a medicinal aerosol formulation containing a particulate drug, a propellant, and a stabilizing agent containing water. The compsitions of the instant claims contain formoterol and a pharmacologically suitable fluid, as defined in the specification, where the composition is stable during long term storage and the fluid contains water. As described in detail above, pharmacologically suitable fluids for use in the instantly claimed compositions do not include propellants. The cited reference does not teach or suggest any compositions that are formulated with a pharmacologically suitable fluid, as defined in the instant specification. Nor does the cited reference teach or suggest replacing the propellants taught therein with a pharmacologically suitable fluid of the instant claims. Thus, one of ordinary skill in the art, given the teachings of the cited references, would not have been motivated to prepare the instant compositions. Absent such motivation, the instant claims are not *prima facie* obvious over the teachings of the cited references.

Therefore, the Office Action has failed to set forth a *prima facie* case of obviousness

In order to establish a *prima facie* case of obviousness, there must be a teaching or suggestion in the cited reference that would have motivated one of ordinary skill in the art to do what applicant has done. Applicant respectfully submits that no such motivation exists in the cited reference. The cited reference teaches compositions that are formulated with a propellant. The instant claims encompass compositions that are formulated in a pharmacologically suitable fluid, as defined in the instant specification. Thus, the compositions of instant claims are not taught or suggested by the cited reference. Therefore, the instant claims are not *prima facie* obvious over the teachings of Adjei *et al.*

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In view of the above remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By: 
Dale L. Rieger
Registration No. 43,045

Attorney Docket No. 18025-1013
Address all correspondence to:
Stephanie Seidman, Esq.
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 7th Floor
San Diego, California 92122
Telephone: 858 450-8400
Facsimile: 858 587-5360
email: sseidman@hewm.com